pathic hemolytic anemia, fever, bizarre neurological symptoms/signs, and renal involvement. The condition is associated with infections, systemic lupus erythematosus (SLE), pregnancy, estrogen therapy, neoplasms, and allogeneic bone marrow transplantation [1–4]. Two patients was diagnosed to have TTP in our department, and both gave a history of using the 17β-estradiol transdermal skin patch as a form of estrogen replacement therapy. As this form of estrogen replacement therapy has not been widely used in our community, its association with a higher risk of developing TTP, as compared to the more conventional oral estrogen therapy, is suspected.

The first patient was a 55-year-old woman had a history of SLE diagnosed 10 years ago. Both renal and cerebral involvement was reported at that time. She responded well to steroid therapy, and the SLE was quite inactive during the last few years. She had been using the 17β-estradiol transdermal skin patch (2 mg twice weekly, equivalent to an effective dose of 25 μg/day) for more than 5 years as estrogen replacement therapy after her menopause. She presented in September 1995 with easy skin bruising, tiredness, and passing dark-coloured urine for about 1 week. Physical examination revealed only the presence of generalised petechiae. The blood counts showed hemoglobin, 8.6 g/dl; white blood cell count (WBC), 6.6×10^9/L; platelet 17×10^9/L; and reticulocyte, 8%. Peripheral blood film revealed polychromasia and numerous schistocytes. Urinalysis showed mild proteinuria and the presence of hemoglobinuria. There was evidence of hemolysis: hyperbilirubinemia, absent serum haptoglobin, and raised methemalbumin.

Renal and liver function tests were otherwise normal. Serum lactate dehydrogenase (LDH) was six times elevated. The coagulation profile including prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and fibrinogen level, were normal and the d-dimer was not raised. The Coombs test was negative and platelet-associated antibody not found. She still had a positive 1 in 360 antinuclear factor and a weakly positive anti-DNA. Serum C3/C4 levels were normal. Bone marrow biopsy revealed erythroid hyperplasia and increased megakaryocytes. A diagnosis of TTP was made. She responded promptly to repeated plasma exchange and fresh frozen plasma infusion with full normalisation of blood counts. Prednisolone 30 mg/day and enteric-coated aspirin 100 mg/day were also given.

The second patient was a 44-year-old woman. She was also using the 17β-estradiol transdermal skin patch (2 mg twice weekly, equivalent to an effective dose of 25 μg/day) for about 6 months, prescribed by her gynecologist for menorrhagia. She presented in July 1993 with fever, headache, and mental confusion. On physical examination, fever, jaundice, pallor, and generalised petechiae were noted. She was mentally confused, but there was no focal neurological sign. Blood counts showed hemoglobin, 7.2 g/dl; WBC count, 15×10^9/L; platelet count, 13×10^9/L; and reticulocytes, 17%. Peripheral blood film revealed polychromasia, numerous schistocytes and the presence of normoblasts. Urinalysis revealed hemoglobinuria. There were also evidences of hemolysis: hyperbilirubinemia, absent serum haptoglobin and raised methemalbumin. The liver function tests were otherwise normal. There were mildly raised serum urea (14.1 mmol/L) and creatinine (0.158 mmol/L). Serum LDH was 10 times elevated. The coagulation profile, including PT, APTT, TT, and fibrinogen level were normal and the d-dimer was not raised. Coombs test was negative and platelet associated antibody not found. Antinuclear factor and anti-DNA were both negative. Bone marrow biopsy revealed erythroid hyperplasia and increased megakaryocytes. A diagnosis of TTP was made. She responded repeated plasma exchange and fresh frozen plasma infusion. There was good neurological recovery, as well as complete normalisation of blood counts.

TTP has been recognized to have a strong association with estrogen therapy [4]. However, there is so far no evicence that any particular estrogen gives a higher risk. TTP is an uncommon disorder. As the major hematology referral centre in Hong Kong seeing hundreds of new cases a year, our department has had only three cases of TTP documented during the past $2\frac{1}{2}$ years, including the two patients described above. The third patient was a man with disseminated adenocarcinoma.

Because of its relatively high cost, the 17β-estradiol transdermal skin patch is not very commonly used in our community. Most of our patients requiring estrogen replacement therapy are using one of the oral preparations. Although the development of TTP in our two patients who were using the skin patch might be purely coincidental, we have the suspicion that the preparation may possibly be associated with a higher risk of the development of TTP. Further reports of similar cases will be useful in substantiating the hypothesis. The 17β-estradiol transdermal skin patch is often prescribed for physiological substitution and is used in postmenopausal women. Transdermal therapy with 17β-estradiol delivers the hormone in unchanged form directly through the skin directly into the bloodstream [5]. It raises the estradiol concentration to a level similar to that of the early to midfollicular phase, maintaining it over the application period. So far, there has been no report of associated coagulopathy or platelet abnormality with the preparation [5]. However, we are not certain as to whether this sustained constant level of estradiol provided by the transdermal system may render patients more susceptible to the development of TTP, especially in those with other risk factors, such as our first patient with SLE. Compared to the oral estrogen preparations, this appears to be a unique feature of the preparation. As TTP remains a rare disorder, further reports of similar cases will be required for confirmation.

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Acute Esophageal Stricture After Induction Chemotherapy for Acute Leukemia

To the Editor: Although dysphagia in patients with acute leukemia is usually related to reflux esophagitis, infectious esophagitis, chemotherapy [1], and leukemic infiltration [2], acute esophageal stricture resulting from chemotherapy in the patient with leukemia is very rare. I report here a patient with acute myelogenous leukemia who developed esophageal stricture within 1 month of chemotherapy.

A 40-year-old man was admitted with right middle lobe pneumonia in July 1995. A complete blood count showed hemoglobin of 8.4 g/dL, a white blood cell count of 4×10^9/L (62% blasts), and a platelet count of 84×10^9/L. The bone marrow examination revealed 5% myeloblasts, 86% promyelocytes, 1% proerythroblasts, 2% basophilic erythroblasts, 3% polychromatophilic erythroblasts, 1% orthochromic erythroblasts, and 2% lymphocytes. Some promyelocytes had multiple Auer rods and were myeloperoxidase positive. He was diagnosed as having acute myelogenous leukemia (AML) M3 and pneumonia. After the resolution of pneumonia, induction chemotherapy consisting of adriamycin (45 mg/m^2 D1-3) and

cytosine arabinoside (100 mg/m^2 D1-7) was commenced. From 3 weeks after induction chemotherapy, he began to complain of epigastric pain, which was not responsive to ranitidine and antacid. Meanwhile, empiric antibiotics and fluconazole were administered for fever and prolonged neutropenia. The bone marrow examination on the 32nd day demonstrated complete remission. In spite of hematologic remission, he had suffered from dysphagia and odynophagia since the 39th day. A fiberoptic esophagoscopy and esophagogram revealed multiple denuded deep ulcerative lesions on mid-esophagus and distal esophageal stenosis of 12 cm in length. Biopsies were taken, and pseudohypae consistent with moniliasis or leukemic infiltration were not found. A Levin tube was inserted for feeding. A fiberoptic esophagoscopy performed 3 weeks later showed disappearance of edema and inflammatory reaction, but still persistent ulcerative lesions and esophageal stenosis were seen. An esophagectomy and esophagogastrostomy was carried out on the 116th day. Histology showed mucosal infiltration of mononuclear cells and transmural fibrosis involving submucosa and the muscle layer.

In this case, it was felt that the duration from the first symptom of reflux esophagitis to dysphagia was too short to develop an esophageal stricture. Bacterial, viral, or fungal infection are associated with mucosal ulcerations but usually not stricture formation, although there was a case report of extensive esophageal stricture following candidiasis resulting from chemotherapy [3]. Furthermore, the empiric antifungal agent, fluconazole, had already been administered before development of dysphagia, and endoscopic biopsy specimens were negative for candida. Consequently this esophageal stricture seems to be a result of chemotherapy, particularly adriamycin. Severe esophagitis resulting in stricture has been reported following adriamycin and radiation therapy for lung cancer [4].

This case suggests that the possibility of esophageal stricture should be considered in symptomatic patients treated with adriamycin-containing chemotherapy, even early in the clinical course.

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